Aus der Universitäts-Kinderklinik (Jennerspital) Bern

Direktor: Prof. Dr. E. Glanzmann

DERMATITIS SEBORRHOIDES IN CHILDREN

(with reference to the treatment of this condition with Biotin and Vitamin F)

INAUGURAL-DISSERTATION

zur

Erlangung der Doktorwürde

der Medizinischen Fakultät

der Universität Bern

vorgelegt von

Marvin Steinhardt

von New York, New York, USA

ARNAUD DRUCK BERN 1956

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Von der Medizinischen Fakultät auf Antrag des Herrn Prof. Dr. E. Glanzmann zum Druck als Dissertation genehmigt.

Bern, den 17. Dezember 1955

Der Dekan der Medizinischen Fakultät:

Prof. Dr. med. W. Wilbrandt

INTRODUCTION

The establishment of Dermatitis Seborrhoides in infants as an entity in itself, clearly distinguishable, both clinically and histologically, from the group of exudative diatheses and other forms of infantile eczema, was due to the work of MORO in 1932. Clinically, it is a disease of the skin appearing within the first three months of life and characterized by the formation of fatty crusts on the scalp ("Cradle Cap" of American authors), eye-brows and axilla. The dermatitis also affects the intertriginous regions of the back, lower abdomen, gluteus and limbs, where scaling is the prominent manifestation. If the fatty crusts, which consist of sebum, desquamated keratin and skin fat ("Gneis" of German authors) are removed, the skin underneath is found to be red and inflamed. Morphologically, the lesions consist of scaling, non oozing papules which become confluent to form plaques of various sizes and shapes. Itching is usually absent, or, if present, very slight. A maj[illegible] of the infants show a definite anemia, signs of disturbed gastro-intestinal functi[illegible] weight. There is no eosino-philia[illegible] Prausnitz-Kustner reaction is negat[illegible] a generalized Erythrodermia Desq[illegible] often fatal form of the dis-ease.

Indi[illegible] hoides began with the work of Gyorgy (14) and concerned [illegible] Vitamin H, later identified as biotin, in the alleviation of symptoms produced in rats fed on a high egg white diet. Since then experimental deficiency syndromes in rats, dogs, and chickens produced by the feeding of a biotin free diet, or by sterilization of the intestinal tract with antibiotics to prevent biotin synthesis by the intestinal flora, or by feeding large amounts of egg white containing avidin, a protein which combines with biotin completely inactivating it, have shown a similarity, both clinically and histologically, with D.S. in infants.

Especially typical were the skin lesions found in rats fed on an egg white diet. At the end of a three to four week period the skin showed an itching, desquamating and exfoliative dermatitis, accompanied by alopecia, seborrhea, discoloration of the fur and fissuring of the skin around the angles of the mouth. Weight loss and inhibition of normal growth were an integral part of this syndrome. Biotin administration had a curative action in an extremely short time. A similar

syndrome was produced by Sydenstricker and his coworkers (40) on four human volunteers fed on a high egg white diet. Within three weeks a seborrhoic eczema appeared and was followed three weeks later by an exfoliative dermatitis and severe neurological symptoms. The biotin excretion in the urine sank from an average of 29 γ to 62 γ per 24 hours at the start of the experiment, to 3.7 γ to 7.3 γ per 24 hours in the sixth week. A coincidental case of an Italian labourer who ate ten to twelve raw eggs and drank one to two liters of wine a day for a period of months was reported by Williams (43). The larourer had a severe dermatitis similar to that produced in biotin deficient rats. Müller (25) reports six cases of infants with D.S. due to ingestion of incorrectly prepared carrots which contained an antibiotin principle similar to avidin. All these cases showed complete and rapid improvement with biotin.

Further support for the biotin hypo- or avitaminosis hypothesis of D.S. is the observation that 80 % of the cases occur in infants fed on mothers milk, which has less of a biotin content than cow milk. The values differ with various authors: Neuweiler and Ritter (26) report 0.16 % to 2.2 %; Laurence et al. (22) report 0.8 % to 3.0 %; Svejcar and Homolka (39) report 1.8 % to 3.0 %. Svejcar and Homolka found also that the biotin values in the blood and urine of normal children compared with the values found in breast fed children suffering with D.S. and E.D.L. were 56 % lower in the sick infants. Amelioration of the disease was concomitant to a rise in the biotin level in the blood. Decreased urinary excretion of biotin in D.S. and E.D.L. has been confirmed by others (3). Additional information has been obtained by an inquiry into the causes of the upsurgence of D.S. during and after the last war. Here again the biotin level in the milk of mothers in areas of undernutrition was distinctly below that of mothers in areas where an increased incidence of D.S. was not noted (42).

All this evidence plus the fact that biotin improves the dermatitis in infants (3, 10, 20, 21, 23, 25, 39, 41, 44) points to a biotin hypo- or avitaminosis as the primary etiological factor in D.S. The deficiency can be caused in a multitude of ways. Decreased intake in breast fed infants has been discussed above. Toxic or infective influences which increase the body's demand for biotin may cause a relative deficiency. Disturbed gastro-intestinal function, so common in these infants, may inhibit the ability of the infantile organism to utilize the available quantities due to poor intestinal resorption or to the production of incomplete protein breakdown products which have an antibiotin or avidin like effect. Lack of other vitamins and factors which work synergestically with biotin and enhance its action must be mentioned. Lemke (21) reports good results in three of four biotin resistant cases of D.S. if Vitamin B_6 is used, and Schreiner et al. (35) describes successful results in D.S. with topically applied Vitamin B_6 ointment.

THERAPY

The therapy in the clinic of Professor Glanzmann can be divided into dietetic, local and specific. The dietetic treatment is concerned with bringing the infant into good nutritional state, the attainment of which is sometimes curative in itself. Fats and NaCl are reduced to a minimum because they have been shown by clinical experience to cause an increase in the severity of the skin manifestations. Penicillin and other antibiotics are used to eliminate all toxic and infective foci, since infections cause an increase of the biotin requirement and an inhibition of its utilization in the body.

The local treatment is consistant with the standard dermatological procedures. Scaling is treated with salicylic acid in a vaseline base and erythrodermic areas are treated with zinc oxide oil and talc. In our use of specific biotin therapy, the F. Hoffmann-La Roche & Co., Basle, product is used. The dose is 2 x 5 mg. i.m. daily, or, in less severe cases, 2 to 4 tablets of 5 mg. daily. The parenteral route is indicated in all cases with disturbed resorption and dyspeptic signs. The results of treatment are measured entirely by the improvement of the clinical picture, since normal blood levels can not be established, due to other factors such as constitution and utilizing ability of the organism. The addition of other B-complex vitamins and of Vitamin C is sometimes advisable.

CASE 1

R.S., 8 weeks old: Pregnancy and birth normal, birth weight 3700 grm. Family history negative. Nutrition: Never breast fed; received Guigoz milk.

Present illness: At age of 10 days, papules appeared around anus and spread to involve gluteal regions, inner side of both thighs, extending down to knees. Treatment with talc and zinc paste was unsuccessful. Admission: 6/5. A 5.100 gm. infant in good nutritional condition. Fatty crusts on the head, eyebrows and eyelashes, and in the axilla. The skin underneath was highly inflamed. In the body creases, gluteal folds, and retroauricular, on the face, neck and trunk were desquamating erythematous areas with papules on their margins. Hands and feet were free. No itching. Physical examination was otherwise negative. Blood normal, except for slight shift to the left. No eosinophilia.

Diagnosis: Dermatitis Seborrhoides Psoriasioid.

Treatment and Course: Diet of Eledon 3 %, Soldor 2 %, Dextropur 3 %: Locally salicylic oil applied to crusted areas, boric acid compresses on the inflamed areas, and daily Pelsano baths. Internally 300'000 units of depot Penicillin for 3 doses on

alternating days and biotin 1 amp. daily i.m. Improvement noticed on the third day after admission and on 10/5 all scaling disappeared. By 14/5 the head was clean and, except for the acutely inflamed gluteal regions, most of the signs of dermatitis had disappeared. The inflamed areas improved with zinc naphthol oil. Complete remission was observed by 12/6, and the infant was given 2 x 1 tablet biotin daily for security. Diet changed to 21 % Pelargon, and infant discharged 17/6 completely healed weighing 6.200 gm.

Summary:

A case of Dermatitis Seborrhoides was treated with a diet of Eledon 2 %, Soldor 2 % and Dextropur 3 %, biotin 1 amp. i.m. daily plus 3 injections of 300'000 units of Penicillin. Local application of boric acid compresses, zinc naphthol, and salicylic oil were used in conjunction with daily Pelsano baths. Improvement was noted after 18 days, and complete cure was effected in 5 weeks, whereupon the patient was discharged.

CASE 2

M.C.B., age 4 months. Pregnancy and delivery normal; weight at birth 3.100 gm. Family history: Father has psoriasis and mother is a diabetic.

Nutrition: Infant breast fed for one month and then Pelargon and later Eledon added.

Present illness: At the age of 3 months, small papules followed by crusting appeared on the head and face. The lesions were dry and showed no exudation. Admission 17/9: a 5.300 gm. infant in good general and nutritional state, well developed for age. On the head, fatty yellowish lamellar crusts, on an acutely inflamed skin base. Some papules evident on the margins. In the inguinal folds the skin deeply reddened. Physical examination was otherwise normal. Blood and urine normal. No eosinophilia.

Diagnosis: Dermatitis Seborrhoides.

Therapy and Course: Diet: Eledon 10 %, Soldor 2 %, Dextropur 5 %. Locally boric in vaseline on the head and daily Linacidin baths. Internally: Biotin 2 x 1 amp. daily i.m., Vi-Nicotyl 2 x 1 tablet daily, Vit. D. "stoss" of 2 x 1/2 total dose. Because of a static weight curve and slight dyspepsia with loose stools, Dextropur 6 % given and then changed to Nutromalt 5 % plus Arobon 3 %. On 24/9, the crusting was gone, and all that remained were a few conglomerations of papules which finally disappeared by 3/10, the skin being completely free of dermatitis. The biotin reduced to 3 x 1 tablet daily. After adding Pelargon, which the infant tolerated very well, the child was discharged with a diet of 5 x Pelargon 21 % and 2 x 1 tablet biotin. The weight on discharge was 5.800 gm.

Summary:

A case of Dermatitis Seborrhoides was given a diet of Eledon 10 %, Soldor 2 %, and Dextropur 5 % and treated with local applications of boric acid vaseline plus daily Linacidin baths. Internally biotin 2 x 1 amp. i.m. daily, Vi-Nicotyl. and a Vitamin D "stoss" was given. Improvement was noted after 7 days, and the infant was discharged completely cured after 3 weeks.

CASE 3

H.M., age 6 weeks. Pregnancy and birth normal. Birth weight 3.650 gm. Family history negative.

Diet: Completely breast fed.

Present illness: On the tenth day of life, the gluteal area became red and scaly. The skin beneath was erythematous. The erythema spread to abdomen, and 10 days before admission, crusts appeared on the brows and on the head. 3 days before admission, the neck and thorax became involved.

Admission: 13/10: A 4.400 gm. infant in a good nutritional state, but moderately reduced general condition. On the head, face and retro-auricular creases especially, but also on the abdomen, inner side of both thighs and legs, perineal and gluteal regions were numerous small and large polycyclic confluent fatty plaques of scaling crusts. The surrounding skin was red and infiltrated. On the back and shoulders the lesions were more psoriasioid. Physical examination revealed a Hernia Inguinalis on the right side. Blood: normal. No eosinophilia.

Diagnosis: Dermatitis Seborrhoides.

Therapy and Course: Diet: Eledon 3 %, Soldor 2 %, Dextropur 3 %. Local: Zink oil and daily baths in Linacidin/Pelsano. Internally: 2 amps. biotin daily i.m. plus 2 tablets. Prophylactically Penicillin 300'000 units was given 5 times on 13/10, 14/10, 17/10, 18/10, 23/10. On 20/10, a significant improvement of the skin was noted. It lost its inflammatory appearance, and the scaling regressed. The general state of the infant improved, and weight gain was noted. The regression of the dermatitis progressed nicely, so that on 9/11, biotin was reduced to 3 x 1 tablet daily. However, the retro-auricular lesions remained resistant but reacted well to zinc naphthol salve and aloplastine ichthamole applications. The course continued well, and the infant was started on Pelargon 19 % on 16/11 and then to Pelargon 21 % 8 days later because of a flattened weight curve. At this time, the skin was completely healed, and the infant was discharged on 29/11 weighing 4.750 gm.

Summary:

A case of Dermatitis Seborrhoides was put on a diet of Eledon 3 %, Soldor 2 % and Dextropur 5 %, given biotin 2 x 1 amp. i.m. daily plus 5 x 300'000 units of penicillin, and treated with local applications of zinc oil, zinc naphthol, and aloplastine ichthamole combined with daily Linacidin/Pelsano baths. After reducing the biotin to 3 x 1 tablet, the infant was discharged completely cured after one month.

CASE 4

A.J., age 6 weeks. Pregnancy and birth normal. Birth weight 2.500 gm/50 cm. Family history negative.

Nutrition: Infant never breast fed. Received Guigoz milk and Maizena.

Present illness: One week before admission, crusts appeared on the head and eyebrows. Three days before admission, the entire body became diffusely reddened, especially the gluteal region, legs, axilla and trunk ascending to the level of the navel.

Admission: 27/11: A 3.400 gm. infant in good nutritional and good general condition. The skin showed fatty yellowish crusts with desquamation. From the hair line extending to the eyebrows and behind the ears down onto the neck, the skin was extremely erythrodermic. In the intertriginous areas and on the abdomen below the navel were fatty scales of typical psoriasioid numular form. Physical examination otherwise normal. Blood and urine normal. No eosinophilia. Hb 80 %, R.B.C. 4.3 million.

Diagnosis: Erythrodemia Desquamativa Leiner (severest form of Dermatitis Seborrhoides).

Therapy and Course: Diet: Pelargon 16 %. Local: Zinc oil, boric acid vaseline, Pelsano baths. Internally: 1 amp. biotin daily i.m. Because of poor stools and vomiting, the diet was soon changed from Pelargon to Eledon 5 %, Soldor 2 %, Dextropur 3 % with 3 % Arobon and then to Eledon 10 % and Dextropur 5 %. Under the above mentioned regime, the skin showed improvement on the third hospital day. The erythrodemia was markedly decreased. On 10/12, the note on the hospital chart stated that the skin was amazingly improved and that the improvement was progressing rapidly. The crusts had disappeared from the head and on 20/12, only the skin of the inguinal regions and the knee joints showed erythrodemia. Biotin tablets 3 x 1 tab. daily replaced parenteral administration. After this rapid regression of the skin changes, improvement became stationary with the inguinal region remaining inflamed. Because of a slight anemia, Hb 72 % and R.B.C. 3.8 million 2 x 1 tablet Ferro-iron daily was started on 28/12. The skin remained the same. Daily zinc talc

powders and Linacidin baths were begun. On 14/1 papules noted when the infant was in contact with damp surroundings, and the child was given daily potassium permanganate baths. On 19/1, the Hb was 85 %, and the iron was stopped. The skin was completely smooth and normal, except for two small areas of pustules which healed in 5 days. From this time until discharge on 3/2, the course was uneventful. The infant discharged on a diet of 17 % Pelargon, and Vit. D. was given for Craniotabes that was noted.

Summary:

A severe case of Erythrodermia Desquamativa Leiner was put on a well tolerated diet of Eledon 5 %, Dextropur 3 %, and Soldor 2 % and given biotin 1 amp. i.m. daily. Local applications of boric acid vaseline and zinc oil combined with daily Pelsano or Linacidin baths were used. Improvement proceded rapidly at first, and an anemia which developed was treated with iron. The infant was discharged with a clear skin and symptom free after 3 months.

CASE 5

R.M., 9 weeks old, 2nd child. Pregnancy and delivery normal. Weight at birth 3.910 gm. Family history: Parents healthy. The mother's brother had "Milk Eczema".

Nutrition: Breast fed for 6 weeks, and from the second week on Guigoz and rice gruel added to diet.

Present illness: 6 weeks prior to admission, the infant had a moderate diarrhea, at which time the gluteal regions became highly inflamed. The attending physician ordered zinc salve with no improvement, and the erythema spread to involve the greater part of the body. Three days before admission, the head became involved. No itching.

Admission: 13/10: A 5.100 gm. infant in a good nutritional state and moderately reduced general condition. The skin exhibited a diffuse scaling erythematous dermatitis. On the gluteal and inguinal regions, in the skin creases, and on the back and face were numerous fatty desquamating lesions which were, for the most part, confluent. Discrete individual lesions were present on the head. The hands, soles of feet and perineal regions were free. Physical examination was otherwise negative. Blood: Normal, except for a slight shift to the left.

Diagnosis: Dermatitis Seborrhoides.

Therapy and Course: Diet: Eledon 10 %, Soldor 2 %, Dextropur 5 %. Local: Zinc oil, aloplastin and ichthymole salve, Linacidin baths daily. Internally: Biotin

2 x 1 amp. daily i.m. Under this regime, the skin improved, the erythema lessened, and the scaling all but disappeared by the eighth hospital day. On 28/10, a dyspepsia with loose mucous stools appeared and Arobon 5 % was added to diet. The skin kept on improving slowly, and by 5/11, biotin 3 x 1 tablet daily and 1 x 1 amp. i.m. were given. The dyspepsia disappeared, and the infant gained weight but behind the ears, oozing patches of dermatitis remained and boric acid compresses were applied. A slight anemia was treated by one tablet of Ferro-Iron daily, and Pelargon 17 % was introduced into the diet. The infant responded well, and it was raised to 4 x Pelargon 21 %. The dermatitis however varied from day to day, but was markedly improved. On 29/11, 2 x 3 drops of Linacidin daily was given. On 7/12, the infant's parents wanted the child discharged. The dermatitis was almost completely healed. On the gluteal fold and perineum, and on the inner aspect of both thighs, a moderate eryhtema with small red papules remained. The child was discharged on 9/12 with a weight gain of 1.600 gm. The mother was given biotin tablets, zinc naphthalan for local use and Linacidin for daily baths and was instructed to continue treatment at home until all skin changes had disappeared.

Summary:

A moderately severe case of Dermatitis Seborrhoides was given a diet of Eledon 10 %, Soldor 2 % and Dextropur 5 % and treated with local applications of zinc oil aloplastine and ichthymole salve, combined with daily Linacidin baths. Biotin therapy was started as 2 x 1 amp. i.m. daily and later reduced to 3 x 1 tab. and 1 x 1 amp. daily. The patient was discharged after 8 weeks with moderate erythema on the thighs and perineum, and the mother was given biotin tablets and instructed to continue therapy at home.

Similar therapeutic results with biotin have been reported by Svejcar, Thelin, Freudenberg, and Glanzmann among others. At this clinic, nine cases of D.S. treated successfully with biotin were reported by Berger (3). Interesting to note was that cases of eczematized dermatitis seborrhoides responded only slightly, if at all, to biotin. A comparison of 15 cases treated at this clinic without biotin and the above mentioned nine cases treated with biotin was made. The cases were carefully selected with regard to clinical condition, so that the comparison would be as fair as possible. The duration of illness in the non biotin treated cases was on the average 7 to 8 weeks as compared to an average of 4 to 5 weeks for those treated with biotin. Of the 15 only 9 improved, while 8 of the 9 biotin treated cases were sent home symptom free. Biotin, therefore, should be given in all cases of simple Dermatitis Seborrhoides in infants.

The role of biotin in human metabolism is not clearly understood. A relationship exists between biotin, folic acid, and pantothenic acid (8). A synergistic effect

with pyridoxine is possible (21). Its action as a coferment as well as its indeterminate action in fat and protein metabolism has been reported (29). The fact that it is efficacious in D. S. proves that it is necessary for normal skin function.

DERMATITIS SEBORRHOIDES ECZEMATISATA

Some cases of D. S. change their character and become eczematized. In place of the dry scaling areas we find inflamed oozing regions of variable shapes and sizes. The papules become pustules and vesicles which eventually burst leaving wet, oozing, raw, erosions on the skin. Itching is a prominent symptom, an eosinophilia, sometimes as high as 50 %, usually appears in the circulating blood, and very often the egg white reaction becomes positive. The regions most severely affected are now the face, cheeks and hands. Unfortunately, these cases are not amenable to biotin therapy. In some cases the infant's hands must be restrained in order to prevent him from scratching himself and causing a severe pyodermic infection. It is perhaps for this reason that Glanzmann (10) classifies two forms of D. S.: a deficiency form constituting a nutritional deficiency of the skin and responding well to therapy: a therapeutically difficult constitutional form which becomes latent, frequently recurs, and often eczematizes.

UNSATURATED FATTY ACIDS

In cases of Dermatitis Seborrhoides eczematisata, we, in this clinic, since biotin has shown itself unsatisfactory, have attempted the use of polyunsaturated fatty acids, a procedure introduced by Hansen (16) for the management of many forms of infantile and adult eczemas.

The first indication that fats are a dietary necessity was the publication of a paper by [illegible] in 1928 (6) entitled: "A new disease produced by the rigid exclusion of fat from the diet". Rats fed on this Burr and Burr diet, consisting of ether and alcohol extracted casein, fat free yeast, sugar, salt, and vitamins A and D, exhibited typical dermatitis, necrosis of the tail, red swollen paws, desquamating dermatitis of the back, alopecia and seborrhea. Growth was arrested, the weight decreased steadily, kidney and genito-urinary signs appeared, and in the 12th week the animals died. The disease was different from the typical manifestations of A or B avitaminosis and was not, as originally thought, a pellagra. Histopathological examination of the animals which died, revealed a thickened and strongly differentiated epidermis with a highly differentiated stratum granulosum accompanied by a thick horny layer.

Healing was brought about by the administration of minimal amounts of lard. The tail and feet lesions healed, the dermatitis disappeared and the rats began to gain weight. Further investigation revealed the active principals in lard to be three polyunsaturated fatty acids of the type linoleic, linolenic, and arachnidonic. Other fatty acids which do not contain 18 carbon atoms and do not have at least two double bounds, are not active. Because only minimal amounts were necessary to improve the condition of the rats, these fatty acids were grouped under vitamins and called Vitamin F. This designation is not accepted universally and American workers, due to the fact that work with radioactive isotopes have shown that these fatty acids can not be synthesized by the body and must be supplied by the diet, have accepted the term "Essential Fatty Acids" (E.F.A.).

The fact that these fatty acids possess a specific action in experimental animals opened up interesting possibilities for their therapeutic use in skin diseases. Hansen (16, 17) indicated that these fatty acids have clinical significance in that infants, children and adults suffering from eczema show definite improvement after being given 30 to 60 grams of bacon daily. Bacon has been shown to be one of the richest sources of the essential fatty acids. The clinical improvement was accompanied by a rise in the iodine number of the blood serum and an increase in the unsaturated fatty acids in the serum. Although the iodine number is affected by factors such as the age of the patient, presence of infection etc., the relationship is beyond doubt significant. Since then, many authors have reported good to excellent results in the treatment of many infantile and constitutional eczemas with bacon and lard (1, 2, 4, 9, 17, 18, 34). Azerad and Grupper (3) question the use of lard because of its variable content of "F active principles" and its difficulty in administration due to its unpalatability. Stangl (37), in an excellent review of the clinical significance of polyunsaturated fatty acids, tabulated the results of ten authors who treated a total of 633 cases of infantile eczema with E.F.A. The results were excellent in 302 cases (47.7 %), improved in 168 cases (26.6 %), and unsatisfactory in 163 cases (25.7 %).

It has not been possible to definitely define clinical symptoms of E.F.A. deficiency in man. However, in prison camps during the last war, it was noted that underfed humans, particularly those who were underfed in fats, exhibited inflammation of the skin and mucous membranes which healed only with difficulty. Infants showed impetigo and eczema. The skin of all the individuals was dry, scaly and gray. The hair was dull, dry, and brittle. These modifications are characteristic of fat deficiency. Diseases due to lack of fat were also observed in towns and cities suffering from wartime food restrictions although the minimum requirements for carbohydrates, proteins, and vitamins had been met satisfactorily. The administration of maize oil, olive oil, lard, and bacon, foods rich in unsaturated fatty acids, produced a noticeable improvement, while commercial fats and foods containing saturated

fatty acids such as myristic, palmitic and stearic, not only were ineffective, but, in many cases, intensified the severity of the skin lesions.

A paper by Berger and Hurni form this clinic (4) reports five cases of D.S. eczematisata treated with a bacon diet and one case treated with "Linacidin", a linoleic-linolenic acid preparation of high potency. All cases responded very well to this therapy. In addition to the ameliorating effect on the skin symptoms, a remarkable improvement in appetite and mood of the infants was noted and the infants gained weight nicely. This is of significance since, as mentioned above, many cases of D.S., and with certain reservations the eczematized cases, have been cured by relieving the dystrophic symptoms so prevalent in these infants. Because of the restricted diet used in D.S., this has been a very difficult problem. With the use of essential fatty acids in the form of bacon or as the commercial preparation "Linacidin", excellent results have been attained.

In this clinic we begin with a daily divided amount of 5 grams of bacon which has been boiled for several hours in salt water and then smoked over night. This improves the taste and makes it more palatable. The bacon is cut into small pieces or ground up with vegetables and fruits and served as a gruel. The amount of bacon is increased progressively depending on the course of the patient, the average amount being 30 grams daily. In some cases, we use "Linacidin". This product is advantageous because it is available as concentrated drops, capsules, bath salts, and ointments. Lately, a parenteral preparation, especially recommended when intestinal function is disturbed, has been prepared. Additional routine dermatological dressings are applied to the skin, antibiotics are used to prevent secondary infections, Vitamins B and G are given, and biotin, 5 to 10 mg. daily, is administered. In some cases "Linacidin" ointment has shown itself of value in the scaling stage of the eczema. "Linacidin" baths are also of value. As in other cases of D.S., the fat in the diet is reduced and low fat milk products such as buttermilk is used. The NaCl in the diet is also reduced to a minimum because of its adverse effect on exudative conditions.

CASE 6

L.B., age 7 1/2 months First child Pregnancy normal and birth 20 days premature. The birth was normal. Birth weight 2,600 gm. Family history negative.

Present illness: Infant entirely breast fed for 3 months, whereupon an "eczema" appeared. The diet was changed to Eledon. At age of 6 months, an inguinal hernia appeared, and it was reduced at a hospital. Since then the diet consisted of no milk, but a mixture of Galactina, oat and rice gruel and fruit in sugar water mornings and before noon; a noon meal of Zwieback in sugar water; a late noon and

evening meal of Galactina. The eczema started as an inflammation of the skin around the eyebrows and by one month before admission, it had become generalized all over the body. The lesions varied from dry and scaly to wet and oozing.

Admission 19/3: A 6.400 gm. infant in a eutropic state. The head was covered with fatty yellow crusts, the skin beneath was moderately red. The entire body was also covered by these crusts and scales. On the trunk, arms and legs, similar individual lesions, partly confluent, were present. The cervical lymph nodes were slightly enlarged and indolent. Physical examination revealed a bilateral inguinal hernia. Blood: R.B.C. 3.7 million, Hb 55 %. W.B.C. was normal, no eosinophilia.

Diagnosis: Dermatitis Seborrhoides Eczematisata; Anemia, Hernia Inguinalis bilateral.

Therapy and Course: Tea, 1 banana and 1 grated apple daily. Locally: Zinc oil. Internally: 2 x 1 tablet biotin daily. The diet was soon changed to two meals of vegetables and two meals of Eledon 5 %, Soldor 2 %, Dextromaltose 3 %. The crusts were removed and the underlying skin appeared red and moderately infiltrated. The crusts on the head were rather resistant to therapy, but the now free skin was treated with 2,5 % zinc naphthol. Improvement continued slowly, but the infant's weight began to sink considerably, so that it was decided to add 5 gm. of bacon to the vegetable mixture. By 8/4, the arms and legs were clean and the face and head were only slightly erythematous. The bacon was raised to 10 gm. and eventually to 20 gm. daily. The weight began to increase. Because of the anemia, blood transfusions of 100 c.c. and 120 c.c. were given on 27/4 and 5/5 respectively. Also due to an outbreak of Varicella on the ward, the infant received 0.5 c.c. of Gamma Globulin. Under a prophylactic protection of 150.000 units of depot Penicillin, the hernia were successfully operated on 9/5 and 28/5. By 19/5 the dermatitis was completely gone, the skin was smooth and of good texture and colour. After another blood transfusion of 100 c.c. on 9/6, the Hb rose to 84 %, and the infant was discharged on 12/6. Weight on discharge: 7.000 gm.

Summary:

An infant with Dermatitis Seborrhoides Eczematisata, anemia and a bilateral inguinal hernia was given a diet of tea, bananas and apples and then Eledon 5 %, Soldor 2 % and Dextromaltose 3 % 2 x 1 amp. of biotin daily i.m., zinc naphthol salve, 5 gms. of bacon, later raised to 20 gms. daily were also prescribed. Complete healing was noted after 8 weeks.

CASE 7

D.E., age 7 months. Third child. Pregnancy and birth normal. Weight at birth 3.650 gm. Family history: Father suffering for years from an eczema of the chest and anus.

Present illness: Completely breast fed until the end of the fourth month. In the fifth month, infant received fruit and vegetable puree and in the sixth month Eledon. At age of 2 months, the infant was hospitalized for 6 weeks because of a pneumococcal meningitis. At this time, the head and face became affected by an itching skin affliction. 3 weeks prior to admission, the redness and crusting spread to involve the trunk and extremities. Was treated with F 99 and a Sulfa salve.

Admission 30/5: A 7.900 gm. infant in a good nutritional state. The skin of the head was covered by a typical eczema which in some parts was covered by crusts and in others was exudating. In addition, many bloody spots due to scratching were seen. The dermatitis extended to trunk, arms and hands. On the trunk, the eczema showed little crusting and the skin around was dry and lichenified. Physical examination was otherwise normal. Blood normal. Eosinophilia 13 %.

Diagnosis: Dermatitis Seborrhoides Eczematisata.

Therapy and Course: Diet: Seledon 2 %, Eledon 5 %, Dextropur 7 %, 1 apple grated daily, Sojabasan 13 %. Locally: Linacidin/Sedothiol salve and daily Pelsano baths. On the second day after admission, the crusts began to disappear, and the lesions on the head were no longer exudating. Therapy continued with Linacidin salve and the eczema improved slowly, but the infant had a large weight lose which by 6/6 amounted to 600 gm. Biotin 1 amp. plus 3 x 1 tablet daily together with 5 gms. of saltfree bacon were added on 21/6 because the dermatitis showed little change. The weight began to increase, and bacon was raised to 10 gm. daily. The dermatitis now improved remarkably, so that on 10/7, only a few small erythematous areas remained on the trunk. The remaining skin was free and no longer irritated. By 19/7 complete disappearance of all signs of skin irritation, and the infant was discharged completely recovered. Weight on discharge 7.300 gms. Pelsano baths and Sedothiol salve was given to mother for use if necessary.

Summary:

A case of Dermatitis Seborrhoides Eczematisata was given a diet of Seledon 2 %, Eledon 5 %, Dextropur 7 %, Sojabasan 13 %, and an apple daily, local Linacidin/Sedothiol salve and daily Pelsano baths. After addition of biotin 1 amp. i.m. plus

3 x 1 tab. daily and 5-10 gms. of bacon, the skin improved remarkably and the patient was discharged after 6 weeks in the hospital.

CASE 8

H.P.S., age 5 months. Pregnancy normal, devilery by a midwife at home. Birth weight 2.940 gms. Family history negative, except for an aunt who has an eczema.

Present illness: Breast fed for 5 weeks, then rice gruel with sugar added to diet. At this time tiny vesicules appeared on the eyebrows. The attending physician ordered Eledon 10 % with rice gruel and sugar and in the tenth week of life Pelegon 21 % was substituted. The dermatitis began to spread from the eyebrows up to the forehead and head and down to the cheeks, arms, legs, and chest. The attending physician ordered Linacidin salve and 3 x 10 drops Linacidin daily. The course was variable, vesicules which broke and oozed finally giving way to crusting. Severe itching was present.

Admission 26/10: A 6000 gms. eutropic infant. On the head and face were thick yellow fatty crusts. The entire face was irritated with numerous scratch marks and blood flecks. The trunk and the extensor surfaces of the extremities were especially affected. Except for the face, the lesions did not exudate. The basic lesions consisted of single confluent plaques covered by dry fatty crusts. The underlying skin was of deep red colour and heavily infiltrated. Physical examination was otherwise normal. Blood: Eosinophilia of 21.5 %.

Diagnosis: Dermatitis Seborrhoides Eczematisata.

Therapy and Course: Diet: Eledon 10 %, Soldor 2 %, Dextropur 5 %, Sojabasan 13 %, saltfree fruit. Local: Boric acid salve and boric acid compresses for the face, daily Pelsano baths. Internal: 2 x 1 amp. biotin daily, 2 x 10 drops Nervefene and 4 x 5 c.c. Pyramidon 1.5 % as sedatives.

In two days, the crusts were removed from the head but it was not until 31/10 that the eczema on the face stopped exudating. Naphthalan 6 % was then applied. By 10/11, the crusts were gone and all exudation had ceased, desquamation was present on the trunk, but the skin in general was still strongly infiltrated. Biotin now given as 1 amp. daily with Vit. D 2 x 10 drops and Arovit 2 x 1/2 amp. daily. Because of the stationary weight curve, Dextropur 10 % was added. The skin improved slightly, but naphthalan had to be stopped because of its irritating effect and was replaced by a mild dusting powder and Vit. T (Goetsch) 3 x 5 drops daily. The dermatitis regressed so that on 27/11 biotin was reduced to 2 x 1 tablet daily. A slight remission occurred behind the ears and on the cheek where exudative

eczematous areas appeared. These were quickly checked by boric acid compresses. The infant was discharged on 5/12 with small areas of infiltrated skin on the trunk and cheeks. The mother was given 18 % naphthalan paste, 1.5 % pyramidon mixture, and Pelsano for daily baths and told to continue treatment at home. Weight at discharge 6.100 gms.

Summary:

A moderately severe case of Dermatitis Seborrhoides Eczematisata was given a diet of Eledon 10 %, Soldor 2 %, Dextropur 5 %, Sojabasan 13 %, local applications of boric acid salve and compresses, daily Pelsano baths, biotin 2 x 1 amp. i.m. daily and sedatives to allay itching. Later, Vit. A + D were given and the infant improved slowly but steadily and was discharged with slightly infiltrated skin on the cheek after 6 weeks.

In cases 7 and 8, Sojabasan - a soybean oil - is used. Soybean oil is digestable, palatable and of the edible fats is very rich in unsaturated fatty acids, especially linoleic acid. Inherent to soybean oil are mixed tocopherols which aid in protecting the unsaturated fatty acids from destruction by oxidation. For these reasons, the use of soybean oils is to be recommended with or instead of bacon in selected cases. Soybean oil is also non allergenic as it contains plant proteins, a fact which is of significance if the allergic nature of eczemas is considered.

Improvement of the nutritional state of the infant, betterment of the appetite, and marked weight gain is the first thing noted. There is a constant parallelism between healing of the skin lesions and improvement of the nutritional state in infants treated with E.F.A. (1, 2). The reason for this must, at the moment, remain a matter of surmise. It is definitely not a caloric effect as shown by experimental work of Berger and Hurni (4). The caloric value of bacon was replaced by other foods of equal caloric worth, and in no case was the eutrophic effect observed. Other bacon fractions, all having equal caloric content, were used, and only those fractions containing the unsaturated fatty acids were effective. The action is no doubt due to the known beneficial effect that unsaturated fatty acids have on carbohydrate metabolism through influence on the phosphorylation processes both in resorption through the intestinal mucosa and in the anaerobic cycle of glucogenesis. Further evidence in this deduction is presented by Cortella who found modifications of carbohydrate metabolism, as shown by the Staub-Traugott double glucose tolerance test, in 34 % of his cases of eczema. After treatment with "Vitamin F 99" (Linacidin), the Staub-Traugott effect was positive. This was confirmed by Schmidt-La Baume in cases of furunkulosis treated with unsaturated

fatty acids. This may, in part, explain why so many cases of D.S. are healed by bringing the infant into an eutrophic condition. The importance of carbohydrate metabolism in dermatoses is not completely understood.

The question also arises as to the value of these fatty acids in fat metabolism. Below will be discussed their action in the oxidation of fats and fatty acids. According to Gschadler and Viollier (47), linoleic acid is the factor necessary for the resorption of fat from the intestine and for the synthesis of saturated fatty acids in the body. These authors further state that the unsaturated fatty acids are resorbed from the intestine as phosphatides (lecithin, cephalin, etc.) and transported as such. It has also been shown that certain organs, among them the skin, need linoleic acid for the formation of their special structural phosphatides.

A direct relationship between biotin and the essential fatty acids has not been reported. The fact that pimelic acid, produced by the oxidation of higher fatty acids and fats, is a basic substance, necessary for the synthesis of biotin by certain bacteria, and that unsaturated fatty acids act as catalysts in the oxidation of fats and higher fatty aicds, may be of significance.

The interplay of various other vitamins is also of interest. Schreiner and his coworkers (34) have treated some cases of D.S. successfully with local applications of pyridoxine. These workers conclude that some cases of D.S. trace their inception to a local metabolic defect in the utilization of Vitamin B_6 by the skin with the lack of essential fatty acids playing an indeterminate but highly important role. Vitamin B_6 internally was of very little use in these cases unless supplementary fatty acids were used. This confirms other reports that the fatty acids are essential for the maintainance of the normal resorptive ability of the skin.

A distinct relationship between pyridoxine and E.F.A. is noted in the results of Birch and Gyorgy (5). These authors were able to show that in cases of acrodynia, a pyridoxine deficiency in rats, a characteristic Burr and Burr dermatitis due to fatty acid deficiency, developed. This dermatitis could not be treated successfully if the fatty acids were not available. Other investigators have treated cases of acrodynia with E.F.A. alone and obtained good results (34). It seems, therefore, that Vitamin B_6 has an economical action on the essential fatty acids (31) or that E.F.A. are necessary for the proper utilization of minimal amounts of Vitamin B_6 by the skin (35). Noteworthy is the fact that it is difficult to produce an acrodynia in rats fed on a diet rich in unsaturated fatty acids. Richardson and Hogan (30) have shown an interaction between the essential fatty acids, pantothenate, and pyridoxine in the treatment of rat dermatitis. Emerson and Wurtz (8) demonstrated the necessity of biotin and folic acid for the proper utilization of pantothenic acid. Vitamin E has been observed to act as an antioxidant, protecting E.F.A. from oxidation in vitro (46).

All this evidence of the interplay of many factors with E.F.A. might indicate that clinical pictures in humans which have been treated successfully with these fatty acids are not primary E.F.A. deficiencies, but rather an interference with the intergration of these various factors in the metabolism.

It is possible that a latent deficiency of E.F.A. can occur as the result of the use of commercial fats. Rats fed on commercial or hydrated fats and oils manifest more severe dermatitis than rats fed on a Burr and Burr fat free diet. Clinical experience in pediatrics has shown that diets high in fats cause an upsurgence of the dermatological lesions. These fats plus insufficient quantities of E.F.A. cause a disturbance of cellulo-tissular formation. The action of the unsaturated fatty acids, according to Schauenstein (33), is to hasten the formation of collagenous and fibrous tissue as well as to hasten the epithelialization by virtue of their affinity for oxygen in a like manner as Vitamin C.

The amount of the essential polyunsaturated fatty acids necessary has been estimated to be 1 % of the normal diet. The therapeutic amount is 5 to 60 grams of bacon (1, 4, 17) of 1.000 to 10.000 Shepard-Linn units of a purified commercial preparation of these acids (12). A Shepard-Linn unit represents the minimum quantity of Vitamin F, which, when applied daily to the skin of the tail of a rat after ten days of the Burr and Burr fat free diet, succeeds in protecting the animal from the symptoms of deficiency which would otherwise be found on the thirtiest day. Hansen and Weise determined normal blood values of E.F.A. for rats and dogs, but difficulty was found in trying to apply the same methods to infants.

Although dermatitis seborrhoides is most probably a biotin deficiency disease, dermatitis seborrhoides eczematisata seems to be another entity more closely related to eczema than to dermatitis seborrhoides. It is in these eczematized cases of D.S. that the essential polyunsaturated acids are most effective even though their absolute lack may not be the primary etiological factor. It is possible that a disturbed skin metabolism is the cause of the eczematous reaction and that the fatty acids, by virtue of their integrated action with other vitamins, enzymes, and perhaps hormones, restore the normal skin integrity. The mode of action of these acids might be in the nature of a conservatory effect for other factors or perhaps a lowering of the tissue sensitivity to deficiency of these factors. For a clear understanding further investigations must be carried out. Be this as it may, clinically speaking, the polyunsaturated fatty acids are a useful adjunct to biotin in the treatment of dermatitis seborrhoides eczematisata. In pure D.S., biotin alone is sufficient in the vast majority of the cases.

SUMMARY

1. Dermatitis Seborrhoides in infants is most probably a biotin deficiency disease, either due to insufficient quantity in the diet, or inability of the infantile organism to utilize the available supply.

2. Excellent results have been obtained in this as well as in other clinics with the use of intramuscular or oral biotin, 5 to 10 mgs. daily, depending on the severity of the case.

3. Polyunsaturated essential fatty acids of the type linolenic, linoleic, and arachidonic (Vitamin F) are effective in the treatment of biotin resistant cases of dermatitis seborrhoides eczematisata. Their activity depends on the fact that they contain 18 carbon atoms and have 2 C=C bindings. They can be used either in the form of 5 to 60 grams bacon daily or as the purified preparation "Linacidin" drops, ampules, ointment, bath salts, and now also available for parenteral administration, or as contained in Soyabean oil.

4. The action of the polyunsaturated fatty acids in D.S. eczematisata is due, at least in part, to the bettering of the nutritional condition of the infant through their effect on carbohydrate and fat metabolism and to the stimulatory effect they have on the process of epithelialization.

5. No distinct relationship between biotin and the polyunsaturated fatty acids has been demonstrated, but synergism of both with pyridoxine and pantothenic acid and perhaps other vitamins is possible so that both biotin and E.F.A. may be effective in D.S. and D.S. eczematisata even though their lack may not be the primary factor.

I am grateful to Professor E. Glanzmann for his aid in preparing this dissertation, and for his kind consent in allowing me the use of case histories from the files of the "Jenner Kinderspital", Berne.

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